Patents

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#12/C
on 4/29/03

In re Application of: **GIBBINS ET AL.**

Application No. **09/675,892**

Filed: **September 29, 2000**

For: **SILVER-CONTAINING COMPOSITIONS, DEVICES AND METHODS FOR MAKING**

Art Unit: **3764**

Examiner: **L.M. Hamilton**

RESPONSE TO OFFICE ACTION

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

Responsive to the Office Action mailed November 21, 2002, to which a reply is due March 21, 2003, by virtue of the Petition for Extension of Time for one month and the $55 fee, Applicants respectfully requests reconsideration of the above-identified application in view of the following amendments and remarks.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, DC 20231, on **March 21, 2003**.

Mary Anthony Merchant, Ph.D. - Reg. No. 39,771

CLEAN COPY OF AMENDMENTS

In the Claims

Please cancel Claim ~~11~~ without prejudice.

Please amend the following claims:

~~10.~~ (Amended) A method of making a matrix, comprising:

(a) combining a hydrophilic polymer, a cross-linking agent, non-gellable polysaccharide

(b) adding in no particular order, a solution of a cation-donating compound, wherein the cations are metal ions, and a solution of an anion-donating compound, wherein the anions are added in excess of the metal cations; and which react to form a metal colloid;

(c) adding a cross-linking catalyst and N,N,N'N'-tetramethylethylene diamine and mixing;

(d) forming the mixture into a desired shape;

and where the metal colloid is directly incorporated in the matrix without the prior incorporation of the metal colloid into another delivery vehicle.

~~12.~~ (Amended) The method of Claim ~~10~~, further comprising adding a hydration control agent.

~~13.~~ (Amended) The method of Claim ~~10~~, further comprising adding a coating agent.

~~14.~~ (Amended) The method of Claim ~~10~~, further comprising before step c, adding a stabilizing solution comprising an electron acceptor having a higher electrochemical potential than the metal cation.

C3

~~18.~~ 17 (Amended) A method for making a hydrophillic matrix having antimicrobial activity, comprising,

directly incorporating a metal colloid in a hydrophillic matrix by forming a metal colloid by adding to the hydrophilic matrix, in no particular order, an organic solvent solution of a cation-donating compound, wherein the cations are metal ions, and an organic solvent solution of an anion-donating compound, wherein the anions are added in excess of the metal cations; such that the association of the metal cation and the anion of the anion-donating compound is favored.

~~19.~~ 18 (Amended) The method of Claim ~~18~~ 17, further comprising adding an active agent, wherein the active agent is selected from the group consisting of antimicrobial agents, antifungal agents, antibacterial agents, anti-viral agents, antiparasitic agents, anaesthetics, mucopolysaccharides, growth factors, proteins, angiogenic factors, wound healing agents and adjuvants.

~~20.~~ 19 (Amended) The method of Claim ~~18~~ 17, wherein the metal colloid comprises silver chloride.

~~21.~~ 7 (Amended) The method of Claim ~~10~~ 1, further comprising adding an active agent before step (c), wherein the active agent is selected from the group consisting of antimicrobial agents, antifungal agents, antibacterial agents, anti-viral agents, antiparasitic agents, anaesthetics, mucopolysaccharides, growth factors, proteins, angiogenic factors, wound healing agents and adjuvants.

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C5

~~31.~~ 21 (New) A biocompatible hydrophilic polymeric antimicrobial matrix, comprising a hydrophilic cross-linked polymer network, and a metal colloid directly incorporated in the matrix, wherein the metal colloid is formed by the reaction of an anionic solution and a metal cationic solution, and wherein the anions of the anionic

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solution are in an excess concentration of the metal cations, such that association of the metal cation and the anion is favored.

22 21
~~32.~~ (New) The matrix of Claim ~~31~~, further comprising a non-gellable polysaccharide.

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23 21
~~33.~~ (New) The matrix of Claim ~~31~~, wherein the anionic solution and the metal cationic solution are made with organic solvents.

24 21
~~34.~~ (New) The matrix of Claim ~~31~~, wherein the metal cation is silver.

25 21
~~35.~~ (New) The matrix of Claim ~~31~~, wherein the metal colloid is a weakly soluble silver chloride colloid.

20 17
~~36.~~ (New) The method of Claim ~~18,~~ further comprising adding in an organic solvent solution, a compound of an electron acceptor having a higher electrochemical potential than the metal of the metal colloid.

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REMARKS

After entry of this amendment, Claims 10, 12-16, 18-36 are pending. Claims 10, 12-14, 18-21, 26 and 27 have been amended and new claims, Claims 31-36, have been added. Support for the amendments and the new claims are found throughout the specification. No new matter has been added.

Based on the following remarks, Applicants respectfully request reconsideration and allowance of the pending claims.

Rejection under 35 U.S.C. § 103(a)

1. Claims 10, 12-13 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Nangia, in view of Friedman. As Examiner Hamilton and Applicant's representative have discussed in the personal interview held January 23, 2003 and in several telephonic interviews, Claim 10, as currently amended, and the claims depending from Claim 10, are allowable over Nangia, in view of Friedman. Thus, Applicants request the Examiner to withdraw this rejection.

2. Claims 11, 14 and 16 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Nangia, in view of Friedman, and further in view of Romans. Claim 11 has been cancelled. As Claim 10 has been found to be allowable over Nangia and Friedman, the teaching of Romans, as stated in the Action, "a composition for use in treating wounds comprising metals, a stabilizing agent and copper chloride" does not render these claims obvious. The teaching of Romans combined with the device disclosed by Nangia does not teach or suggest Applicant's currently pending invention. Applicants request the Examiner to withdraw this rejection.

3. Claim 15 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Nangia, Friedman, Romans and further in view of Hara. As Claim 10 has been found to be allowable over Nangia and Friedman, the teaching of Romans in combination with the teaching of Hara of a solution of ferric chloride does not render this claim obvious. The teaching of a stabilizing solution that is an alternative of one taught by Romans, combined with the device disclosed by Nangia does not teach or suggest Applicant's currently pending invention. Applicants request the Examiner to withdraw this rejection.

4. Claims 18-22 and 24-30 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Nangia in view of Romans and Friedman. The Action stated that "Nangia discloses the invention substantially as claimed, however Nangia does not disclose a stabilizing solution, sustained release of the active agent, the agent being metal or salt, tetracycline or penicillin." With entry of the amendments to Claim 18, Applicant's currently claimed invention is not taught or suggested by the cited art.

Claim 18 and dependent Claims 19 and 20 are directed to a method of making an antimicrobial matrix. As agreed, Nangia does not teach Applicant's invention as currently claimed in that Nangia does not teach the direct incorporation of agents into a matrix. Neither Romans nor Friedman teach a two-step method of forming a metal colloid directly in the matrix by the addition of the cation of the colloid and the anion of the colloid, and by providing the cation and the anion solutions in an organic solvent. Neither individually, nor in combination do the references provide a teaching or suggestion that renders Applicants' presently claimed invention obvious.

Claims 21, 22, 24-30 are dependent claims which depend from Claim 10, and provide further characteristics of disclosed matrices. As agreed, Claim 10, as currently amended, and the claims depending from Claim 10, are allowable over Nangia, in view of Friedman. The additional teachings of Romans and Friedman do not provide sufficient teaching or suggestion such that when combined with Nangia,

render Applicants' currently claimed invention obvious. Applicants request that this rejection be withdrawn.

5. Claim 23 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Nangia, Romans and Friedman, as applied above to Claim 21, and further in view of Edelman. Claim 23 depends from Claim 21, which is a dependent claim of Claim 10, which is allowable. The addition of the teaching of Edelman, of growth factors, does not provide a teaching or suggestion of Applicants' currently pending invention that alone or in combination with the cited art would render Applicants' currently pending claims obvious. Applicants request the Examiner to withdraw the rejection.

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10. (Amended) A method of making a matrix, comprising:

(a) combining a hydrophilic polymer, a cross-linking agent, non-gellable polysaccharide [and one or more active agents]

(b) adding in no particular order, a solution of a cation-donating compound, wherein the cations are metal ions, and a solution of an anion-donating compound, wherein the anions are added in excess of the metal cations; and which react to form a metal colloid;

(c) [(b)] adding a cross-linking catalyst and N,N,N'N'-tetramethylethylene diamine and mixing;

(d) [(c)] forming the mixture into a desired shape;

[(c) pouring the mixture into molds to form sheets;

(d) dehydrating and re-hydrating the sheets;]

and where the [one or more active agents are] metal colloid is directly incorporated in the matrix without the prior incorporation of the [active agent] metal colloid into another delivery vehicle.

12. (Amended) The method of Claim 10, further comprising [the addition of] adding a hydration control agent.

13. (Amended) The method of Claim 10, further comprising [the addition of] adding a coating agent.

14. (Amended) The method of Claim 10, further comprising before step c, [the addition of] adding a stabilizing solution [to stabilize the active agent] comprising an electron acceptor having a higher electrochemical potential than the metal cation.

18. (Amended) A method for making a hydrophillic matrix having antimicrobial activity, comprising,

[(a)] directly incorporating a metal colloid in a hydrophillic matrix by forming a metal colloid by adding to the hydrophilic matrix, in no particular order, [an anion-donating solution and a cation-donating solution to a polymeric matrix to form an active agent within and/or on the polymeric matrix] , an organic solvent solution of a cation-donating compound, wherein the cations are metal ions, and an organic solvent solution of an anion-donating compound, wherein the anions are added in excess of the metal cations; such that the association of the metal cation and the anion of the anion-donating compound is favored.

[; and (b) adding to the polymeric matrix a stabilizing solution; and

wherein the matrix allows for the sustained release of the active agent.]

19. (Amended) The method of Claim 18, further comprising adding an [wherein the] active agent, wherein the active agent is selected from the group consisting of antimicrobial agents, antifungal agents, antibacterial agents, anti-viral agents, antiparasitic agents, anaesthetics, mucopolysaccharides, growth factors, proteins, angiogenic factors, wound healing agents and adjuvants [comprises a metal or metal salt].

20. (Amended) The method of Claim [19] 18, wherein the metal [salt] colloid comprises silver chloride.

21. (Amended) The method of Claim 10, further comprising adding an active agent before step (c), wherein the active agent is selected from the group consisting of antimicrobial agents, antifungal agents, antibacterial agents, anti-viral agents,

antiparasitic agents, anaesthetics, mucopolysaccharides, [metals,] growth factors, proteins, angiogenic factors, wound healing agents and adjuvants.

26. (Amended) The method of Claim 10, wherein the [polymeric matrix] hydrophilic polymer comprises a natural or synthetic polymer.

27. (Amended) The method of Claim 10 further comprising adding a water loss control agent, a plasticizer, and a hydration control agent.

31. (New) A biocompatible hydrophilic polymeric antimicrobial matrix, comprising, a hydrophilic cross-linked polymer network, , and a metal colloid directly incorporated in the matrix, wherein the metal colloid is formed by the reaction of an anionic solution and a metal cationic solution, and wherein the anions of the anionic solution are in an excess concentration of the metal cations, such that association of the metal cation and the anion of the anionic solution is favored.

32. (New) The matrix of Claim 31, further comprising a non-gellable polysaccharide.

33. (New) The matrix of Claim 31, wherein the anionic solution and the metal cationic solution are made with organic solvents.

34. (New) The matrix of Claim 31, wherein the metal cation is silver.

35. (New) The matrix of Claim 31, wherein the metal colloid is a weakly soluble silver chloride colloid.

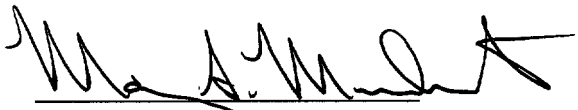
36. (New) The method of Claim 18, further comprising adding in an organic solvent solution, a compound of an electron acceptor having a higher electrochemical potential than the metal of the metal colloid.

CONCLUSION

The foregoing is a complete response to the Office Action mailed November 21, 2002. Applicants respectfully submit that the present application is in condition for immediate allowance. An early notification is earnestly solicited. If the Examiner has any questions, or further issues remain to be resolved, the Examiner is requested to contact the undersigned at (404) 745-2426.

No additional fees are believed due; however, the Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, to Deposit Account No. 11-0855.

Respectfully submitted,



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